

# Papers and Originals

## Factors Influencing the Onset of Chronic Respiratory Disease

W. W. HOLLAND,\* M.D., B.Sc.; T. HALIL†; A. E. BENNETT,‡ M.B., D.I.H.  
A. ELLIOTT,§ M.D., D.P.H.

*British Medical Journal*, 1969, 2, 205-208

**Summary:** To investigate the effect of different environmental and personal factors on ventilatory function 10,971 children resident and going to school in four areas of Kent were examined. Details of past respiratory illnesses were obtained by a questionnaire completed by the parents; the examination included measurement of height, weight, and peak expiratory flow.

Area of residence, social class, family size, and a past history of pneumonia, bronchitis, or asthma were found to be associated with differing levels of peak expiratory flow. These four factors acted independently, and the effects were additive. It is suggested that environment in the early years of life can produce adverse changes which may exist throughout life and contribute to the development of chronic respiratory disease.

### Introduction

Current opinion in Great Britain (Fry, 1961; Scottish Home and Health Department, 1963) suggests that the child who suffers from repeated respiratory infection can be expected to improve as he becomes older and not develop chronic respiratory disease in middle or old age. Harnett and Mair (1963) were unable to show a diminution in mean peak expiratory flow rate in a group of children labelled as "catarrhal" by Mackenzie in St. Andrews in the 1920s as compared with a control group. They were, however, able to trace and follow up only about 67% of the original group.

By contrast, McDonald *et al.* (1958) showed the serious consequences of respiratory infection in childhood in young Royal Air Force recruits, while Reid and Fairbairn (1958) showed that postmen who were invalided from the Post Office because of disabling bronchitis had an excess in both the frequency and the duration of attacks of bronchitis going back to early adult life. Rosenbaum (1961) showed that Army recruits coming from polluted industrial towns suffered more respiratory infections while in the Army than those coming from rural areas, independent of the area in which they were serving. Further suggestion that early exposure to the British urban atmosphere carried a lasting risk of death from respiratory disease is also evident in the excess of lung cancer deaths in British immigrants in New Zealand (Eastcott, 1956) and South Africa and Australia (Dean, 1964) compared with native-born men with similar smoking habits.

The effect of an urban environment in the aetiology of respiratory disease in childhood has been shown by Wahdan

(1963), Douglas and Waller (1966), Reid (1966), and Lunn *et al.* (1967). These studies show that environmental factors such as the parents' social class and the area of residence influence the frequency of respiratory illnesses and levels of ventilatory function. In addition, levels of ventilatory function are lower in children who have had lower respiratory tract infections compared with those who have not.

Such studies, however, have not been able to separate the effect of the different environmental factors on the development of respiratory disease in childhood and have not been able to disentangle the effects of personal constitutional factors from environmental factors. In order to attempt to separate the influence of personal and environmental factors on the development of respiratory disease, we have studied histories of respiratory illnesses and levels of ventilatory function of schoolchildren resident and going to school in four areas of Kent: (1) Rochester, (2) Malling Rural District, (3) Tonbridge, and (4) Cranbrook, Tenterden, and Romney Marsh Rural Districts. These areas contained sufficient numbers of schoolchildren to make meaningful analyses possible, and each area showed some differences in environmental conditions (Tables I and II).

TABLE I.—*Characteristics of the Four Kent Areas (1961 Census)*

	Area 1. Rochester	Area 2. Malling	Area 3. Tonbridge	Area 4. Cranbrook
Persons per acre ..	12.6	0.9	4.8	0.3
Persons per room ..	0.64	0.64	0.60	0.59
Percentage of persons at more than 1½ per room	2.5	3.4	1.8	3.2
Hot-water tap lacking (% total dwellings) ..	25.14	32.94	24.86	22.71
Cold-water tap lacking (% total dwellings) ..	0.23	1.33	0.20	2.40
Fixed bath lacking (% total dwellings) ..	19.22	28.79	21.99	20.55
Water closet lacking (% total dwellings) ..	0.82	9.06	2.07	9.15

TABLE II.—*Levels of Smoke (µg./cu. mm.) in Three Kent Areas for Winter Months 1966-7*

	Area 1. Rochester 4		Area 2. Malling (Snodland)		Area 3. Tonbridge	
	Av.	H.D.	Av.	H.D.	Av.	H.D.
November 1966 ..	80	155	38	98	49	141
December " ..	67	265	35	139	59	282
January 1967 ..	96	221	50	140	70	177
February " ..	75	194	34	133	50	148
March " ..	28	54	12	28	21	52

Av. = Average of all daily concentrations. H.D. = Highest daily concentration.

### Method

In Kent all children going to local authority schools are normally examined by school medical officers at ages 5, 11, and 14. Into this examination procedure was introduced a special examination in the four areas during 1964 and 1965.

\* Professor.

† Research Assistant.

‡ Senior Lecturer.

Department of Clinical Epidemiology and Social Medicine, St. Thomas's Hospital Medical School, London S.E.1.

§ County Medical Officer, Kent County Council.

Before the examination the parents of each child were asked to complete a questionnaire on the child's respiratory symptoms and illnesses since birth, the occupation of the father and the mother, the place of birth of the child, and the number of siblings. At the medical examination the questionnaire was collected from the parent and checked for completeness. If a parent did not attend the examination and the questionnaire was found to be incomplete, a visit to the home was made by a health visitor in order to obtain the desired information. The medical officer measured height and weight, examined the ears and tonsils, measured the peak expiratory flow rate with a Wright Peak Flow Meter, inquired about smoking habits, and recorded school absence. A list of all children who should have been included in the medical examination was obtained from the school staff, who also gave details of attendance at the medical examination and the reason for any absentees.

Twelve medical officers performed the examinations in the four areas, and all were trained in the techniques to be used. To assess the degree of observer variability one standard observer visited each of the 12 medical officers on two or more occasions during the period of study. At this visit the children examined by the medical officer were re-examined by the standard observer. The variation between each medical officer and the standard observer was measured, and, as expected, some observers differed from the standard observer. Nevertheless, none of the differences found between observers can account for the differences to be described. In addition, three of the medical officers worked in two areas and one medical officer worked in three areas. Where differences in prevalence of signs or symptoms or levels of peak expiratory flow rate have been found between areas, these were also found within the group examined by each of the four medical officers.

As the examinations were carried out over a two-year period the data were examined for seasonal variation. The differences described cannot be accounted for by seasonal variations.

## Results

Table III shows the number of children examined and the response rate. Almost 94% of the children residing and attending school in the survey areas were examined. There is little difference in the response rate between areas.

TABLE III.—Number of Children Examined in the Four Study Areas, With Percentage Response Rates

Children Examined	Area 1. Rochester	Area 2. Malling	Area 3. Tonbridge	Area 4. Cranbrook	Total
No. ..	3,698	2,847	1,875	2,551	10,971
% ..	94.6	93.9	92.3	94.2	93.9

This report is limited to examination of variations found in peak expiratory flow rates. Peak expiratory flow rate varies with the age, height, and weight of the child. Since the children in different areas and in different social class groups varied in both height and weight, and since the examinations were performed at slightly different ages, for comparison the peak expiratory flow rate for each age and sex group has been adjusted to a uniform age, height, and weight by using a multiple linear regression equation (see Statistical Appendix). The differences to be described are not due to the method of adjustment, as they also exist in the raw data within the various age, height, and weight groups.

Levels of peak expiratory flow in the four different areas are shown in Table IV. In most of the age and sex groups the levels of peak expiratory flow are lower in Rochester than in other areas. Levels tend to be highest in Tonbridge. The statistical significance of the differences between the areas in peak expiratory flow rates is shown at the bottom of the table. Thus in boys aged 5–8 years there are highly significant differences between Rochester and Malling, Rochester and Tonbridge, and Rochester and Cranbrook. There are also highly significant

TABLE IV.—Mean Peak Expiratory Flow Rates in Different Age, Sex, and Area of Residence Groups (P.E.F.R. Adjusted to Uniform Age, Height, and Weight Within Each Age and Sex Group)

	5–8 Years		9–13 Years		14+ Years	
	M	F	M	F	M	F
1. Rochester ..	120.1	117.8	291.3	268.7	364.9	314.9
2. Malling ..	130.8	126.7	282.4	258.3	363.1	328.4
3. Tonbridge ..	158.3	151.7	309.8	293.9	388.4	367.3
4. Cranbrook ..	134.0	129.4	298.3	268.9	366.6	336.9
Significance:	R M T C	R M T C	R M T C	R M T C	R M T C	R M T C
1 = P < 0.05 ..	3 3 3 R	3 3 3 R	2 3 1 R	2 3 – R	– 3 – R	2 3 3 R
2 = P < 0.01 ..	3 – M	3 – M	3 3 M	3 2 M	3 – M	3 – M
3 = P < 0.001 ..	3 T	3 T	2 T	3 T	3 T	3 T

TABLE V.—Mean Peak Expiratory Flow Rates in Different Age, Sex, and Social Class Groups (P.E.F.R. Adjusted to Uniform Age, Height, and Weight Within Each Age and Sex Group)

Social Class	5–8 Years		9–13 Years		14+ Years	
	M	F	M	F	M	F
I and II = (A) ..	134.6	133.2	301.8	275.1	366.6	344.8
III = (B) ..	133.5	128.3	294.3	270.6	370.3	331.6
IV and V = (C) ..	130.6	127.2	289.6	271.5	364.8	327.5
Significance:	A B C	A B C	A B C	A B C	A B C	A B C
1 = P < 0.05 ..	– – A	2 2 A	1 2 A	– – A	– – A	2 2 A
2 = P < 0.01 ..	– – B	– – B	– – B	– – B	– – B	– – B
3 = P < 0.001 ..	– – B	– – B	– – B	– – B	– – B	– – B

cant differences between Tonbridge and Malling and between Tonbridge and Cranbrook. Differences between Malling and Cranbrook are not statistically significant.

Levels of peak expiratory flow tend to be higher in the children of social class I and II parents compared with those of social class IV and V parents (Table V). These differences are statistically significant in the girls aged 5–8, boys aged 9–13, and girls aged 14 years or more.

TABLE VI.—Variations in Mean Peak Expiratory Flow Rate (P.E.F.R. Adjusted for Age, Height, and Weight in Each Age and Sex Group Separately) and History of Attacks of Bronchitis

Age in Years	Sex	No. of Attacks of Bronchitis				Significance
		0	1	2	3 or More	
5–8	M	135.0	127.5	126.9	124.2	0 1 2 3 0 3 2 3 1 – – – 2 – – –
	F	130.0	125.3	126.2	117.0	0 1 2 3 0 1 – 3 1 – – 1 2 – – –
9–13	M	296.7	288.7	282.6	277.4	0 1 2 3 0 1 1 2 1 – – – 2 – – –
	F	272.8	263.3	255.6	274.5	0 1 2 3 0 1 1 – 1 – – – 2 – – –
14+	M	370.2	359.6	352.7	358.4	0 1 2 3 0 1 – – 1 – – – 2 – – –
	F	335.6	315.8	320.7	320.9	0 1 2 3 0 3 – – 1 – – – 2 – – –

Significance: 1 = P < 0.05. 2 = P < 0.01. 3 = P < 0.001.

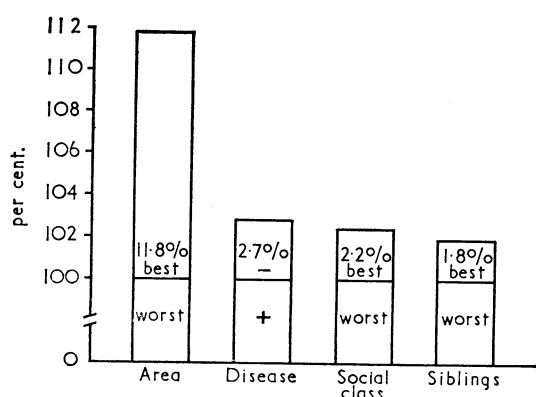
A further factor associated with reduced levels of peak expiratory flow in these children is size of family. Children coming from large families tend to have lower levels than children from small families.

Of the various respiratory illnesses reported, only a past history of pneumonia, bronchitis, or asthma is associated with reduced levels of peak expiratory flow. This is shown in Table VI, which gives the variation in mean adjusted peak expiratory flow rate according to the history of attacks of bronchitis. Children who have not had bronchitis tend to have higher levels of peak expiratory flow than children with a history of one or more attacks. These differences are significant in all age and sex groups.

It is not possible from these results to show whether each of the factors—area of residence, social class, size of family, past history of respiratory illness—exerts an independent effect on levels of peak expiratory flow in these children. The differences between areas may be influenced by differences in the distributions of social class in the four areas; differences between social classes may be influenced by different proportions within each social class living in the different areas. Attacks of pneumonia are influenced by social class, and attacks of bronchitis appear to be influenced by both social class and area of residence.

In order to establish whether the findings as shown are due to interaction or whether each factor exerts an independent effect on levels of peak expiratory flow, further examination of the data was undertaken by analysis of variance with the method of fitting constants (Stevens, 1948). The first stage was to discover what type of model was required—that is, to establish whether the effects of the factors are additive or multiplicative (see Statistical Appendix). The results of the analysis of variance after allowing for non-orthogonality showed that the effects are additive and not multiplicative. Thus the effect of each factor can be assumed to be independent of the others, and the effect of any two or more factors working together is no more than the sum.

The second stage of the analysis of variance was to obtain estimates of the numerical values of the constants and thus to assess the relative effect of each of the four factors. This is represented in the Chart, which gives the finding for one age



Percentage difference in peak expiratory flow rate between best and worst area, social class, siblings, and positive and negative disease (bronchitis or pneumonia). Kent school-children aged 9-13, both sexes.

group. The greatest difference is found between areas and between children who have or have not had bronchitis or pneumonia. The influence of social class and family size is of less importance. The highest percentage of the variation on each age and sex group is explained by the area factor. The statistical significance of the influence of each of the four factors on peak expiratory flow rate in each age and sex group is shown in Table VII. It may be seen from this that the influence of area of residence is significant in each age and sex

group, as is the influence of a history of bronchitis and/or pneumonia. Influence of the parents' social class is significant in all age and sex groups, except for girls aged 9-13 and boys aged 14-16. The influence of family size is statistically significant only in the youngest age group and in boys aged 14-16.

TABLE VII.—Significance of Influence of the Four Factors on P.E.F.R.

	5-8 Years		9-13 Years		14-16 Years	
	M	F	M	F	M	F
Area	***	***	***	***	***	***
Bronchitis and/or pneumonia	***	***	***	***	*	**
Social class	*	**	**	—	—	**
Family size	*	*	—	—	*	—

\*\*\*  $P < 0.001$ . \*\*  $P < 0.01$ . \*  $P < 0.05$ . —  $P > 0.05$ .

The significant effect of social class on peak expiratory flow rate was confirmed by a simple regression analysis. Social classes were ordered in an equal interval linear scale and were allocated the values -1, 0, +1 for social classes I+II, III, IV+V respectively. The direction and the gradient of the trend for each age and sex group obtained from regressing peak expiratory flow rate on social class agreed very closely with the constants obtained.

## Discussion

The findings of this study show that peak expiratory flow rate in childhood is influenced by environmental and personal factors in the form of area of residence, social class, family size, and past history of respiratory disease. These factors operate independently and exert their effect additively.

Before accepting these findings further consideration must be given to possible sources of error. These must include, in addition to observer and seasonal variation and method of adjustment of peak expiratory flow rates which have already been dealt with, the representativeness of the population studied and the accuracy of reporting past illnesses. The number of children normally resident in the four areas but going to special schools was determined. The number of children with respiratory disabilities was small and the findings would not have been invalidated, as more children with respiratory disabilities went to special schools from Rochester than from any of the other areas. Conversely, the greatest proportion of children going to private schools, and thus not examined, was in Tonbridge. Their presence in the study group would therefore be more likely to emphasize the differences found.

The reporting of past illnesses was obviously dependent on recall by the parents, and this might have been influenced by social class or area. No bias was found in the reporting of past ear disease or tonsillectomy in the different social class or area groups, as judged by correspondence between findings at examination and the parents' answers to the questionnaire. Some illnesses are likely to have been wrongly described as bronchitis or pneumonia when they were simply upper respiratory tract infections. Again the differences found in peak expiratory flow rate according to past history are likely to be minimized by any such errors. It is possible that illnesses described as bronchitis might well have been asthma, but the prevalence of asthma found in this study agrees very well with other studies.

The most important of the environmental factors considered is the area of residence. Undoubtedly the children of Rochester showed the lowest levels of peak expiratory flow independent of parents' social class, family size, and past history of respiratory illness. Unfortunately the methods of assessing the various components involved in area of residence are rather crude. It was possible to obtain the levels of smoke and  $\text{SO}_2$  measured at comparable sites in three of the study areas—Tonbridge, Malling, and Rochester. Unfortunately the measurements for the other rural area were not obtainable. Table II shows that

average daily concentrations of smoke were consistently highest in Rochester, lowest in Malling, with Tonbridge in between. The pattern for  $\text{SO}_2$  was very similar. Other measurable components of area of residence such as indices of crowding and qualities of housing such as availability of cold water, hot-water, baths, indoor lavatories, etc. (Table I) show that crowding was greater in Rochester than in any of the other areas but that housing conditions were similar in Rochester and Tonbridge and worse in the rural areas, with Malling worst of all. It is thus tempting to conclude that differences found between the other areas were due in part to housing conditions.

Any such conclusion must be viewed, however, in the knowledge that the four factors—area of residence, social class, family size, and past history—shown in this analysis to be significantly associated with reduced levels of peak expiratory flow account for only some 10–15% of the total variation. However, the degrees of freedom associated with the residual variation are of the order of 2,000, and, though the greater part of the total variation is still to be accounted for, other factors are likely to prove numerous. This implies that the four factors considered in this analysis are of importance. Possibly, however, host factors (Orie, 1961) may have a greater role than has previously been considered.

Cigarette smoking has, of course, been omitted from this report. Previous work (Holland and Elliott, 1968) has shown differences in the prevalence of symptoms in children who smoke compared with those who do not. No differences in levels of peak expiratory flow could be shown in children who smoke compared with non-smokers. This is not surprising, as most of the children who admitted to smoking could have done so for only a relatively short period and therefore insufficient time had elapsed for measurable damage to the respiratory tract to have occurred.

The findings of this study suggest that the environment in the early years of life can produce adverse changes in ventilatory function as measured by the peak expiratory flow rate. These changes possibly remain throughout life and contribute to the later development of chronic respiratory disease. The effect of lower respiratory tract infections, in particular bronchitis, and their significance in childhood should be more widely appreciated.

### Statistical Appendix

The reported peak expiratory flow rates were adjusted according to the formulae:

5–8 years	Male	$Y_s = Y + 3.72(5-u) + 3.95(43-x) + 0.94(43-z)$
	Female	$Y_s = Y + 4.53(5-u) + 3.01(43-x) + 0.56(43-z)$
9–13 years	Male	$Y_s = Y + 1.09(11-u) + 4.54(57-x) + 0.43(82-z)$
	Female	$Y_s = Y + 12.15(11-u) + 6.69(57-x) + 0.43(82-z)$
14–16 years	Male	$Y_s = Y + 6.11(14-u) + 9.27(62-x) + 0.54(112-z)$
	Female	$Y_s = Y - 0.01(14-u) + 6.57(62-x) + 0.37(112-z)$

Where  $Y_s$  = adjusted peak expiratory flow rate,  $Y$  = recorded peak expiratory flow rate,  $u$  = age in years,  $x$  = height in inches, and  $z$  = weight in pounds.

The peak expiratory flow rate can be described by the model

$$Y_{hijk} = \mu + A_1(h) + A_2(i) + A_3(j) + A_4(k) + \epsilon_{hijk}$$

where  $\mu$  is a constant,  $A_1(h)$  ( $h=1, 2, 3, 4$ ) is one of four constants according to the area of residence,  $A_2(i)$  ( $i=1, 2, 3, 4$ ) is one of four constants according to the number of siblings,  $A_3(j)$  ( $j=1, 2, 3$ ) is one of three constants according to social class,  $A_4(k)$  ( $k=1, 2$ ) is one of two constants according to whether the child was reported to have had bronchitis and/or pneumonia, and  $\epsilon_{hijk}$  is an independent random variable.

In Stevens's iterative procedure no restrictions are imposed on the constants  $A_p$ ,  $p=1, 2, 3, 4$ , and therefore the constants are to some extent arbitrary. The differences, however, between the levels of the same factor remain unaltered.

This work was supported in part by a grant from the Department of Health and Social Security. The investigation has been made possible by the support and help of many people, in particular the staffs of the Kent County Council in the health and teaching services. In particular, the medical and health visiting staffs have devoted considerable energy and time to this project. Our thanks are also due to Mr. H. S. Kasap for his advice and to Mr. S. G. Nicholas for the preparation of punch cards. The results were analysed at the Imperial College Centre for Computing and Automation.

### REFERENCES

- Dean, G. (1964). *Proceedings of the Royal Society of Medicine*, 57, 984.  
 Douglas, J. W. B., and Waller, R. E. (1966). *British Journal of Preventive and Social Medicine*, 20, 1.  
 Eastcott, D. F. (1956). *Lancet*, 1, 37.  
 Fry, J. (1961). *The Catarrhal Child*. London, Butterworth.  
 Harnett, R. W. F., and Mair, A. (1963). *Scottish Medical Journal*, 8, 175.  
 Holland, W. W., and Elliott, A. (1968). *Lancet*, 1, 41.  
 Lunn, J. E., Knowelden, J., and Handyside, A. J. (1967). *British Journal of Preventive and Social Medicine*, 21, 7.  
 McDonald, J. C., Wilson, J. S., Thorburn, W. B., Holland, W. W., and Andrews, B. E. (1958). *British Medical Journal*, 2, 721.  
 Orie, N. G. M. (1961). In *Bronchitis: An International Symposium*, edited by N. G. M. Orie and H. J. Sluiter, p. 43. Assen, Van Gorcum.  
 Reid, D. D. (1966). In *Bronchitis: 2nd International Symposium*, edited by N. G. M. Orie and H. J. Sluiter, p. 313. Assen, Van Gorcum.  
 Reid, D. D., and Fairbairn, A. S. (1958). *Lancet*, 1, 1147.  
 Rosenbaum, S. (1961). *British Journal of Preventive and Social Medicine*, 15, 61.  
 Scottish Home and Health Department (1963). *Bronchitis: Report of a Sub-Committee of the Standing Medical Advisory Committee*. Edinburgh, H.M.S.O.  
 Stevens, W. L. (1948). *Biometrika*, 35, 346.  
 Wahdan, M. H. M. E.-H. (1963). *Atmospheric Pollution and Other Environmental Factors in Respiratory Disease of Children*. Ph.D. Thesis. London University.